

Docket No.: HUI-040CP Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF REPLACEMENT SHEET

10 20 30 40 50 60 HUMAN MGIVEPGCGDMLTGTEPMPGSDEGRAPGADPQHRYFYPEPGAQDADERRGGGSLGSPYPG SEQ ID NO:2 SEQ ID NO:4 MOUSE MGIVEPGCGDMLTGTEPMP-SDEGRGPGADQQHRFFYPEPGAQDPTDRRAGSSLGTPYSG 10 20 30 40 50

> MGIVEPGCGDMLTGTEPMP SDEGR PGAD QHR FYPEPGAQD CONS RR G SLG PY G

70 80 90 100 110 GALVPAPPSRFLGAYAYPPRPQAAGFPGAGESFPPPADAEGYQPGEGYAAPDPRAGLYPG SEQ ID NO:2 HUMAN SEQ ID NO:4 GALVPAAPGRFLGSFAYPPRAQVAGFPGPGEFFPPPAGAEGYPPVDGYPAPDPRAGLYPG MOUSE 60 70 80 100 110

> CONS GALVPA P RFLG AYPPR Q AGFPG GE FPPPA AEGY P GY APDPRAGLYPG

130 140 150 160 170 180 HUMAN PREDYALPAGLEVSGKLRVALNNHLLWSKFNQHQTEMIITKQGRRMFPFLSFTVAGLEPT SEO ID NO:2 SEQ ID NO:4 PREDYALPAGLEVSGKLRVALSNHLLWSKFNQHQTEMIITKQGRRMFPFLSFTVAGLEPT MOUSE 120 130 140 150 160 170

> CONS PREDYALPAGLEVSGKLRVAL NHLLWSKFNQHQTEMIITKQGRRMFPFLSFTVAGLEPT

190 200 220 210 230 240 SEQ ID NO:2 HUMAN SHYRMFVDVVLVDQHHWRYQSGKWVQCGKAEGSMPGNRLYVHPDSPNTGAHWMRQEVSFG SEO ID NO:4 SHYRMFVDVVLVDQHHWRYQSGKWVQCGKAEGSMPGNRLYVHPDSPNTGAHWMRQEVSFG MOUSE 180 190 200 210 220 230

> CONS SHYRMFVDVVLVDQHHWRYQSGKWVQCGKAEGSMPGNRLYVHPDSPNTGAHWMROEVSFG

250 260 270 280 290 300 HUMAN KLKLTNNKGASNNVTOMIVLOSLHKYOPRLHIVEVNDGEPEAACNASNTHIFTFOETOFI SEO ID NO:2 MOUSE SEQ ID NO:4 KLKLTNNKGASNNVTQMIVLQSLHKYQPRLHIVEVNDGEPEAACSASNTHVFTFQETQFI 240 250 260 270 280 290

> CONS KLKLTNNKGASNNVTQMIVLQSLHKYQPRLHIVEVNDGEPEAAC ASNTH FTFQETQFI

App No.: 10/008264 Docket No.: HUI-040CP Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF REPLACEMENT SHEET

SEQ ID NO:2 SEQ ID NO:4	HUMAN MOUSE 3	::::::	:::::::::::::::::::::::::::::::::::::::	*******	:::::::::::::		350 360 NCQFLGGDHYSPLLP ::::::: NCQLLGGDPFSPLLS 350
	cons	AVTAYQ	NAEITQLKIC)NNPFAKGF	RENFESMY SV	DTS PSPPGPI	NCQ LGGD FSPLL
SEQ ID NO:2 SEQ ID NO:4	HUMAN MOUSE 3	*****		**** *	::::::::::::	********	410 420 PAFLPSAPGPTMSYY S:::::::::::::::::::::::::::::::::
	CONS	NQYPVPS	SRFYPDLPGQ	KD Q	WLG PR HSY	EAEFRAVSMKF	P LPSAPGPT YY
SEQ ID NO:2	HUMAN MOUSE 42	* * * * * * * *		:::::::::	.:::::::::	1.11 1.11 .	470 480 GPEDQGPPLVWTEI : : : : : : : : : : : : : : : : : : :
	CONS	RGQ VLA	LPGAGWPVAP	QYPPKM PA	A WFRPMRTLP	M PG G SE	G PWE
SEQ ID NO:2 SEQ ID NO:4	HUMAN MOUSE CONS	TSLOPEP	SDSGLGEGD' 490	IKRRRISPY	PSSGDSSSPA 510	GAPSPFDKETE 520	GQFYNYFPN 530
	COMB	25	PPGPGPGD	MININ DEI	FOOGUDODPA	gapspfdke <u>e</u>	age intern

Fig. 1B

Docket No.: HUI-040CP

App No.: 10/008264 Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF REPLACEMENT SHEET

SEQ ID NO:1	EITTM'S BY	10	20	30	40	50	60
	HOMAN	ATGGGCATCGTGGA	sccgggTTgcg	GAGACATGCT		GAGCCGATG	
SEQ ID NO:3	MOUSE	ATGGGCATCGTGGA	SCCGGGCTGCG	GAGACATGCT	GACCGGCACC	GAGCCGATGC	:: :::G
		10	20	30	40	50	
		70	80	90	100	110	120
SEQ ID NO:1	HUMAN	AGCGACGAGGGCCC					
SEQ ID NO:3	MOUSE		GGGGCCCGGA	GCGGACCAAC	:::: :: : AGCATCGTTT	::::::::: CTTCTATCCC	GAGCCG
		60 70	80	90	100	110	
		130	140	150	160	170	180
SEQ ID NO:1	HUMAN	GGCGCGCAGGACGC				STCTCCCTAC	CCGGGG
SEQ ID NO:3	MOUSE	GGCGCACAGGACCC			GCAGCCTGGG(JACGCCCTAC	· · · · · · · · · · · · · · · · · · ·
		120 130	140	150	160	170	
SEQ ID NO:1		190	200	210	220	230	240
_	HUMAN	GGCGCCTTGGTGCC	;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;	AGCCGCTTCC1			
SEQ ID NO:3	MOUSE	GCGCCCTGGTGCCT		3TCGCTTCCT1	GGATCCTTC	CCTACCCGC	CCCGG
		180 190	200	210	220	230	
gro to vo.1		250	260	270	280	290	300
SEQ ID NO:1	HUMAN	CCCCAGGCGGCCGG	CTTCCCCGGC(CTTCCCGCCG:	CCCGCGGAC	3CCGAG
SEQ ID NO:3	MOUSE	GCTCAGGTGGCTGG			CTTCCCGCCG	CCCGCGGGT	CGGAG
		240 250	260	270	280	290	
SEQ ID NO:1	******	310	320	330	340	350	360
	HUMAN	GGCTACCAGCCGGG		CCGCCCCGGA:::::::::			
SEQ ID NO:3	MOUSE	GGCTACCCGCCCGT	GGATGGCTAC	CTGCCCTGA	.CCCGCGCGCG	GGGCTCTAC	CAGGG
		300 310	320	330	340	350	
				•			
	*****	370	. 380	390	400	410	420
SEQ ID NO:1	HUMAN	CCGCGTGAGGACTA					
SEQ ID NO:3	MOUSE	CCGCGCGAGGACTA			GGTGTCTGGG	:: ::::::: AAGCTGAGAG	TCGCG
		360 370	380	. 390	400	410	

App No.: 10/008264 Docket No.: HUI-040CP Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF REPLACEMENT SHEET

SEQ ID NO:1	HUMAN MOUSE	430 440 450 460 470 480 CTCAACAACCACCTGTTGTGGTCCAAGTTTAATCAGCACCAGACAGA
SEQ ID NO:1	HUMAN MOUSE	490 500 510 520 530 540 AAGCAGGGACGCGGATGTTCCCATTCCTGTCATTTACTGTGGCCGGGCTGGAGCCCACC ::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	550 560 570 580 590 600 AGCCACTACAGGATGTTTGTGGACGTGGTCTTGGTGGACCAGCACCACTGGCGGTACCAG ::::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	610 620 630 640 650 660 AGCGGCAAGTGGGAGGCAGGCAGGCAGGCAGGCAAACCGCCTGTAC ::::::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	670 680 690 700 710 720 GTCCACCCGGACTCCCCCAACACAGGAGCGCACTGGATGCGCCAGGAAGTTTCATTTGGG ::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	730 740 750 760 770 780 AAACTAAAGCTCACAAACAACAAGGGGGGCGTCCAACAATGTGACCCAGATGATTGTGCTC :::::::::::::::::::::::::::::::
SEQ ID NO:1	Human Mouse	790 800 810 820 830 840 CAGTCCCTCCATAAGTACCAGCCCCGGCTGCATATCGTTGAGGTGAACGACGGAGAGCCA :::::::::::::::::::::::

Fig. 1D

App No.: 10/008264 Docket No.: HUI-040CP

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Title: T-BET COMPOSITION AND METHODS OF USE THEREOF REPLACEMENT SHEET

SEQ ID NO:1	Human Mouse	850 860 870 880 890 900 GAGGCAGCCTGCAACGCTTCCAACACGCATATCTTTACTTTCCAAGAAACCCAGTTCATT :::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	910 920 930 940 950 960 GCCGTGACTGCCTACCAGAATGCCGAGATTACTCAGCTGAAAATTGATAATAACCCCTTT :::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	970 980 990 1000 1010 1020 GCCAAAGGATTCCGGGAGAACTTTGAGTCCATGTACACATCTGTTGACACCAGCATCCCC ::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	1030 1040 1050 1060 1070 1080 TCCCCGCCTGGACCCAACTGTCAATTCCTTGGGGGAGATCACTACTCTCCTCCTACCC ::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	1090 1100 1110 1120 1130 1140 AACCAGTATCCTGTTCCCAGCCGCTTCTACCCCGACCTTCCTGGCCAGGCGAAGGATGTG :::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN	1150 1160 1170 1180 1190 1200 GTTCCCCAGGCTTACTGGCTGGGGGCCCCCCGGGACCACAGCTATGAGGCTGAGTTTCGA : : : : : : : : : : : : : : : : : : :
SEQ ID NO:1	HUMAN MOUSE	1210 1220 1230 1240 1250 1260 GCAGTCAGCATGAAGCCTGCATTCTTGCCCTCTGCCCCTGGGCCCACCATGTCCTACTAC ::::::::::::::::::::::::::::::

Docket No.: HUI-040CP

App No.: 10/008264 Docket No.: HUI-040CP Inventor: Laurie H. GLIMCHER et al.
Title: T-BET COMPOSITION AND METHODS OF USE THEREOF

REPLACEMENT SHEET

SEQ ID NO:1	HUMAN	1270 1280 1290 1300 1310 1300 CGAGGCCAGGAGGCCTGGGAGCTGGCTGGCCTGTGGCACCCCAGTACCCTGGAGCCAGCC	
SEQ ID NO:1	HUMAN MOUSE	1330 1340 1350 1360 1370 13 AAGATGGGCCCGGCCAGCTGGTTCCGCCCTATGCGGACTCTGCCCATGGAACCCGGCC ::::::::::::::::::::::::::::	,
SEQ ID NO:1	HUMAN MOUSE	1390 1400 1410 1420 1430 14 GGAGGCTCAGAGGACCAGAGGACCAGGGTCCCCCTTGGTGTGGACTGAGA ::: :::::::::::::::::::::::::::::::	:
SEQ ID NO:1	HUMAN MOUSE	1450 1460 1470 1480 1490 15 GCCCCCATCCGGCCGGAATCCAGTGATTCAGGACTGGGCGAAGGAGACTCTAAGAGGA :::::::::::::::::::::::::::::::	• •
SEQ ID NO:1	HUMAN MOUSE	1510 1520 1530 1540 1550 156 CGCGTGTCCCCCTATCCTTCCAGTGGTGACAGCTCCTCCCCTGCTGGGGCCCCTTCTCC : : :::::::::::::::::::::::::	CT
SEQ ID NO:1	HUMAN MOUSE	1570 1580 1590 1600 TTTGATAAGGAAGCTGAAGGACAGTTTTATAACTATTTTCCCAACTGA ::::::::::::::::::::::::::::::::::::	

Fig. 1F

CONS

Docket No.: HUI-040CP

Inventor: Laurie H. GLIMCHER et al.
Title: T-BET COMPOSITION AND METHODS OF USE THEREOF

ANNOTATED SHEET

SEQ ID NO:2	HUMAN	MGIVEP	10 GCGDMLT	2) GTEPMP) ISDEGR	30 ADGADD	OHDVEVI	40	50 ADERRGGGS	60
SEQ ID NO:4	MOUSE	* * * * * * *	::::::::	GTEPMP	:::::	.::::	QHRFFYI		PTDRRAGSS 50	11.11 1
	CONS	MGIVEP	GCGDMLT	GTEPMP	SDEGR	PGAD	QHR. FYI	PEPGAQD	RR G S	LG PY G
SEQ ID NO:2	HUMAN	GALVPA	70 PPSRFLG <i>I</i>)8 Iqqyaya	RPQAAGI	90 FPGAGE	1 SFPPPAI	LOO DAEGYQPO	110 SEGYAAPDP	120 RAGLYPG
SEQ ID NO:4	MOUSE	GALVPAI	APGRFLGS 70	FAYPPI	AQVAGI	FPGPGE 90	FFPPPAG	::::: AEGYPPV 100	DGYPAPDP 110	RAGLYPG
	CONS	GALVPA	P RFLG	AYPPE	Q AGI	PG GE	FPPPA	AEGY P	GY APDP	RAGLYPG
SEQ ID NO:2	HUMAN	PREDYAL	130 SPAGLEVS	140 GKLRVA	LNNHLI	150 WSKFN(1 IMETQHQ	.60 :ITKQGRR	170 MFPFLSFT	180 VAGLEPT
SEQ ID NO:4	MOUSE 12	PREDYAL	:::::::	::::::	LSNHLI	:::::	e:::::: Ohotemi	:::::::	MFPFLSFT	
	CONS	PREDYAI	PAGLEVS	GKLRVA	L NHLI	wskfn(QHQTEMI	ITKQGRR	MFPFLSFT	VAGLEPT
SEQ ID NO:2	HUMAN MOUSE 18	SHYRMFV	:::::::	::::::	SGKWVQ ::::: SGKWVQ	::::::	SMPGNR :::::: SMPGNR		230 PNTGAHWMF :::::::: PNTGAHWMF 230	
	CONS	SHYRMFV	DVVLVDQ	HHWRYQ	SGKWVQ	CGKAEG	SMPGNR	LYVHPDS	PNTGAHWMF	QEVSFG
SEQ ID NO:2	HUMAN	KLKLTNN	250 KGASNNV	260 TQMIVL	QSLHKY	270 QPRLHI	VEVNDG	80 EPEAACN	290 ASNTHIFTF	300 QETQFI
SEQ ID NO:4	MOUSE 24	KLKLTNN	KGASNNV 250	TQMIVL 26	QSLHKY	OPRLHI 270	VEVNDG	EPEAACS 280	::::::: ASNTHVFTF 290	GETQFI

Fig. 1A

KLKLTNNKGASNNVTQMIVLQSLHKYQPRLHIVEVNDGEPEAAC ASNTH FTFQETQFI

App No.: 10/008264 Docket No.: HUI-040CP

Inventor: Laurie H. GLIMCHER et al.
Title: T-BET COMPOSITION AND METHODS OF USE THEREOF

ANNOTATED SHEET

SEQ ID NO:2	HUMAN	AVTAY	310 QNAEIT	OLKID	320 NNPFA	KGFR	330 Enfesm	VTSVD	340 TETE			o Tagni	IVOD	360
SEQ ID NO:4	MOUSE 3	:::::		:::::	:::::	:::: KGFR	::::::	: . : : :	::.:	SPPC	PNCQI	::::	.::	::
	CONS	AVTAY	QNAEIT	QLKID	NNPFA	KGFR	enfesm	y svd	TS P	SPPG	PNCQ	LGGD	FSP	LL
SEQ ID NO:2	HUMAN		370 PSRFYPI				390 WLGAPRI			AVSM			PTM	420 SYY
SEQ ID NO:4	MOUSE 3		PSRFYPI 370		PKDMI 380	SQPY	WLGTPRI 390	ehsye	AEFR 40	AVSM	KPTLL	PSAPG 10	PTV	PYY
	CONS	NQYPV	PSRFYPI	DLPGQ	KD	Q Y	WLG PR	HSYE	AEFR	avsm	KP L	PSAPG	PT	YY
•														
SEQ ID NO:2	HUMAN	RGQEV	430 LAPGAGV	VPVAP	440 QYPPKI	MGPA:	450 SWFRPMF	RTLPM	460 EPGP	GGSE	47 GRGPE	DQGPP	LVW	
SEQ ID NO:4	MOUSE 42	RGQDVI	LAPGAGV 430	VPVAP(QYPPKI 440	MSPAC	WFRPMF 450	RTLPMI	DPGL 46	GSSE	EQG	SSP 47		
	CONS	RGQ VI	Lapgagv	VPVAP(QYPPKI	M PA	WFRPMR	RTLPM	PG (G SE	G	P	W	E
														•
SEQ ID NO:2	HUMAN	APIRPI	490 ESSDSGI		500 SKRRRV							YNTFPI	N.	
SEQ ID NO:4	MOUSE	TSLOPI 480	PSDSGL		KRRRI	SPYE		SPAGA 510	LPSP1	FDKE: 520	regofy	YNYFPI 530	-	
	CONS	PI	SDSGL	.GEGD	KRRR	SPYE	SSGDSS	SPAGA	PSPI	PDKE	EGQFY	MYFP	1	

Docket No.: HUI-040CP

Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF ANNOTATED SHEET

SEQ ID NO:1	HUMAN MOUSE	10 20 30 ATGGGCATCGTGGAGCCCGGGTTGCGGAGACATG ::::::::::::::::::::::::::::::::::::	::::: :::::::::::::::::::::::::::::::::	GATGCCGGGG ::::::: GATGCCG
SEQ ID NO:1	HUMAN MOUSE	70 80 90 AGCGACGAGGGCCGGGCGCCTGGCGCCGACCC ::::::::::::::::::::::::::::	::::::::::::::::::::::::::::::::::::::	ACCCGGAGCCG
SEQ ID NO:3	HUMAN MOUSE	130 140 150 GGCGCGCAGGACGCGGGGGGGGGGGGGGGGGGGGGGGG	::::::::::::::::::::::::::::::::::::::	CTACCCGGGG
SEQ ID NO:1	HUMAN MOUSE	190 200 210 GGCGCCTTGGTGCCCGCCCCCCCCGAGCCGCTTC :::::::::::::::::::::::::::::::	TTGGATCCTTCGCCTAC	CCCGCCGCGA
SEQ ID NO:1	HUMAN MOUSE	250 260 270 CCCCAGGCGGCCGGCCGGCCGGCGCGGCGAG ::::::::::	TTCTTCCCGCCGCCGC	GGACGCCGAG
SEQ ID NO:1	HUMAN MOUSE	310 320 330 GGCTACCAGCCGGGCGAGGGCTACGCCGCCCCG ::::::::::::::::::::::::::::	::::::::::::::::::::::::::::::::::::::	111111 111
SEQ ID NO:1	HUMAN MOUSE	370 380 390 CCGCGTGAGGACTACGCGCTACCCGCGGGACTG ::::::::::::::::::::::::::::::::::::	GAGGTGTCTGGGAAGCT	11: 11:11:

Fig. 1C Fig. 1B

App No.: 10/008264 Docket No.: HUI-040CP

Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF

ANNOTATED SHEET

SEQ ID NO:1	HUMAN	430 440 450 460 470 480 CTCAACACCACCTGTTGTGGTCCAAGTTTAATCAGCACCAGACAGA
SEQ ID NO:3	MOUSE	CTCAGCAACCACCTGTTGTGGTCCAAGTTCAACCAGCACAGACAG
SEQ ID NO:1	HUMAN MOUSE	490 500 510 520 530 540 AAGCAGGGACGGCGGATGTTCCCATTCCTGTCATTTACTGTGGCCGGGCTGGAGCCCACC :::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	550 560 570 580 590 600 AGCCACTACAGGATGTTTGTGGACCTGGTGGACCAGCACCACTGGCGGTACCAG ::::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	610 620 630 640 650 660 AGCGGCAAGTGGGTGCAGTGTGGAAAGGCCGAGGGCAGCATGCCAGGAAACCGCCTGTAC ::::::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	670 680 690 700 710 720 GTCCACCCGGACTCCCCCAACACAGGAGCGCACTGGATGCGCCAGGAAGTTTCATTTGGG ::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	730 740 750 760 770 780 AAACTAAAGCTCACAAACAAGGGGGGCGTCCAACAATGTGACCCAGATGATTGTGCTC :::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	790 800 810 820 830 840 CAGTCCCTCCATAAGTACCAGCCCCGGCTGCATATCGTTGAGGTGAACGACGAGAGCCA ::::::::::::::::::::::::

Fig. 1D Fig. 1B (continued)

Docket No.: HUI-040CP

Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF ANNOTATED SHEET

SEQ ID NO:1	HUMAN MOUSE	GAGGCTGCCT	::: ::::	CCAACAC			890 900 AAACCCAGTTCATT :::::::: AGACCCAGTTCATT 890
SEQ ID NO:1	HUMAN	GCAGTGACTG	::::::::	ATGCCGAG	** *****		950 960 ATAATAACCCCTTT : :::::::: ACAACAACCCCTTT 950
SEQ ID NO:1	HUMAN MOUSE	GCCAAAGGAT	::::::::::	ACTTTGAG	TCCATGTAC	ACATCTGTTG.	1010 1020 ACACCAGCATCCCC : ::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	TCGCCACCTG	BACCCAACT	TCAATTC	* * * * * * * * * *	:: :: ::	1070 1080 CTCCTCTCCTACCC ::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	AACCAGTATCO	TGTTCCCA	ECCGCTTC		**** ****	1130 1140 AGGCGAAGGATGTG :::::::: AGCCCAAGGATATG 1130
SEQ ID NO:1	HUMAN MOUSE	ATCTCACAGCC	TTACTGGCT	:::::	CCCCGGGACC	ACAGCTATGA	.90 1200 GGCTGAGTTTCGA ::::::::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	** ** ****	::::::::::::::::::::::::::::::::::::::	ATTCTTG	CCTCTGCCC	CTGGGCCCAC	250 1260 CATGTCCTACTAC :::::::: TGTGCCCTACTAC 1250

Fig. 1E-Fig. 1B (continued)

Docket No.: HUI-040CP

Inventor: Laurie H. GLIMCHER et al.

Title: T-BET COMPOSITION AND METHODS OF USE THEREOF
ANNOTATED SHEET

SEQ ID NO:3	HUMAN MOUSE	1270 1280 1290 1300 1310 1320 CGAGGCCAGGAGGCCTGGCACCTGGAGCTGGCTGGCCTGTGGCACCCCAGTACCCTCCC ::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	1330 1340 1350 1360 1370 1380 AAGATGGGCCCGGCCAGCTGGTTCCGCCCTATGCGGACTCTGCCCATGGAACCCGGCCCT ::::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	1390 1400 1410 1420 1430 1440 GGAGGCTCAGAGGACCAGAGGACCAGGGTCCCCCCTTGGTGTGGACTGAGATT ::::::::::::::::::::::::::::::::
SEQ ID NO:3	HUMAN MOUSE	1450 1460 1470 1480 1490 1500 GCCCCCATCCGGCCGGAATCCAGTGATTCAGGACTGGGCGAAGGAGACTCTAAGAGGAGG :::::::::::::::::::::::::::::
SEQ ID NO:1	HUMAN MOUSE	1510 1520 1530 1540 1550 1560 CGCGTGTCCCCCTATCCTTCCAGTGGTGACAGCTCCTCCCCTGCTGGGGCCCCTTCTCCT : ::::::::::::::::::::::::::
SEQ ID NO:3	HUMAN MOUSE	1570 1580 1590 1600 TTTGATAAGGAAGCTGAAGGACAGTTTTATAACTATTTTCCCAACTGA ::::::::::::::::::::::::::::::::::::